Dr. David Sayre, sayre@xray1.physics.sunysb.edu
Physics Dept. , SUNY, Stony Brook NY 11794
427 Monroe St., Bridgewater NJ 08807-3093
(908) 595-6854

The Oversampling Phasing Method

D. Sayre, Physics Dept., SUNY, Stony Brook NY11794, and
J. Miao, SLAC, Stanford University, Stanford CA 94309.

In the last few years significant changes have arisen in our perception of the phase problem, among them the concept that finer-than-Nyquist sampling of the diffraction intensity may in the future become of major importance. This in turn coincides with a shift from almost exclusive interest in crystals as the main type of material suitable for structure determination, to a recognition that crystals may not always be available in the future for the ever larger biostructures of interest. In non-crystal situations Bragg sampling loses its meaning, but Nyquist sampling has meaning in both.

Nyquist sampling* is always as fine or finer than Bragg sampling**. Thus finer-than-Nyquist sampling results in more data than Bragg sampling; hence the term "oversampling". The result is more information about the structure, and a positive effect on the phase problem in both the non-crystal and crystal cases. A phasing technique employing the added information uses the fact that when phases are correct Fourier transforming the oversampled data produces zero density outside the specimen envelope. A Fienup-type algorithm, see J. Fienup, Appl. Opt. 21, 2758-2769 (1982), can be used to push that density to zero. Appropriate conditions on the complex density inside the envelope can also be applied. Empirically the oversampling should be such as to produce a somewhat larger volume outside than inside the envelope.

Important new imaging possibilities may result from the non-necessity of crystals. Potential specimens range from single molecules to biological cells, as well as microcrystals*** and crystals with imperfections to be viewed. Also data can, but are not required to, extend to atomic resolution.

Experimentally, measurement of oversampled datasets requires large x-ray exposures, increasing the problem of specimen damage. Cryoprotection of cells can assist, but for molecular imaging at atomic or near-atomic resolution higher-technology data acquisition methods, e.g. femtosecond FEL x-ray pulses, see R. Neutze et al., Nature 406, 752-757 (2000), will be needed.

Based on earlier work in crystallography and in other fields, oversampling was explicitly proposed (1) for x-ray imaging in the non-crystal case. The proposal for the crystal case has also recently been made (2). The necessary excess of sampling over Nyquist fineness has been examined by

several authors and recently has been somewhat lowered (3). 2D tests on simulated (4) and experimental (5) x-ray data have been published. A successful test on a simulated femtosecond-pulse large-protein 3D data set has been carried out (6).

Our group at SUNY has as its main project the 3D imaging of a yeast cell by the technique (7); we hope this will serve as an example of how x-ray diffraction may in the future contribute to cell biology. Our presentations will discuss some of the numerous questions, including cryo-protection of the specimen, large-scale 3D data assembly, missing-data problem, complex scattering density, and quality of the phasing obtained, which are involved in this project.
Simultaneously at Stanford the emphasis is on single-molecule protein work with FEL x-ray pulses.

*Sampling interval inversely related to the size of the diffracting volume.
**Sampling interval inversely related to the size of a crystal unit cell.
***Finer-than-Bragg sampling suffices for this case.

(1) D. Sayre, in Proceedings of 1990 Erice School, pp. 353-356, Plenum (1991).
(2) J. Miao & D. Sayre, Acta Cryst. A56, 596-605 (2000).
(3) J. Miao, D. Sayre & H.N. Chapman, J. Opt. Soc. Am. A15, 1662-69 (1998).
(4) D. Sayre, H.N. Chapman & J. Miao, Acta Cryst. A54, 232-239 (1998).
(5) J. Miao, P. Charalambous, J. Kirz & D. Sayre, Nature 400, 342-344 (1999).
(6) J. Miao, K. Hodgson & D. Sayre, in preparation.
(7) D. Shapiro, poster paper this meeting.

Added March 23 Note added in response to Spence/Fenner suggestion on communication

The central point of our paper is a call for sampling more finely in diffraction space than the finenesses (Bragg or Nyquist) which suffice for reconstruction when phases are known: when the phases are not known the added fineness helps greatly in finding them.

Question: How many of the abstracts do, and how many do not, already have that point built in?

Added April 11 In response to the above, Abraham Szoke has called my attention to (8) and (9), which propose two very interesting additional concepts (items 3 and 4 of his abstract) for eliciting and exploiting oversampling in the crystal case.

(8) A. Szoke, Time resolved holographic diffraction at atomic resolution, Chem. Phys. Letters 313, 777-788 (1999).
(9) A. Szoke, Diffraction of partially coherent X-rays and the crystallographic phase problem. Acta Cryst. A, to be published.